Tubular Handling of K^+ by the Renal Tubule

The normal rate of k^+ filtration is about 756 mEq/day (GFR x plasma K^+ level = 180 x 4.2). Fig. (4-14) illustrates the fate of the filtered K^+

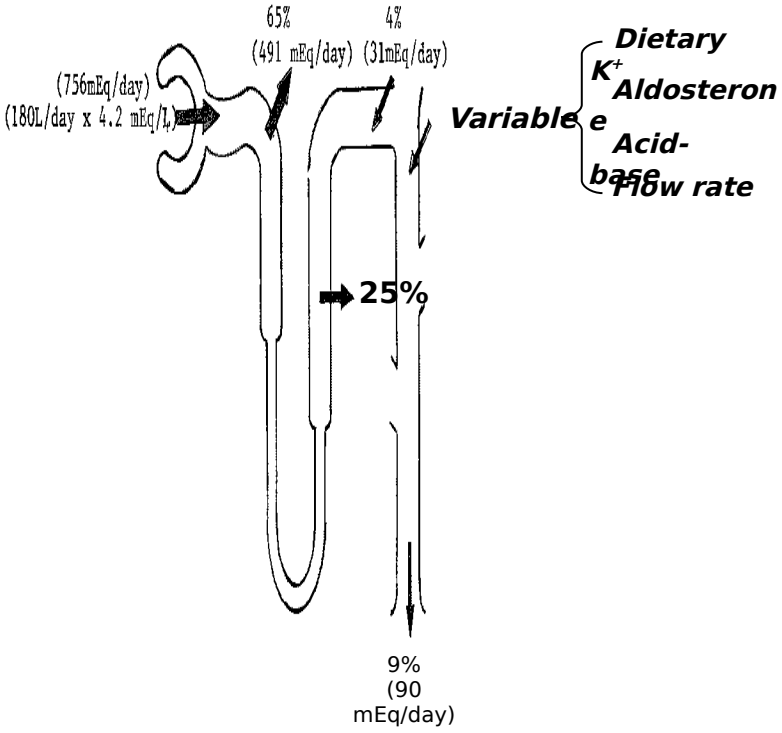


Fig. (4-14): Renal tubular sites of K^+ reabsorption and secretion

- **K^+ is both reabsorbed and secreted by the renal tubule**
- **K^+ Reabsorption:**

1) PCT: Reabsorption of 65% of the filtered K^+

2) Thick ascending limb of the Loop of Henle*:*

25% of the filtered load of K^+ are actively co-transported with Na^+ and Cl^-.

3) Distal tubule and Collecting Tubule*:*

Reabsorb or secrete K^+ depending on dietary intake.

Reabsorption of K^+: involves H^+-K^+ ATPase in the luminal

membrane of intercalated cells.

5% of the filtered load of K^+ is actively reabsorbed by intercalated cells by ATP dependent K^+ - H^+ antiporter in the luminal membrane and exits through K^+ channels in the basolateral membrane. Occurs only on a low K^+ (K^+ depletion). (Fig 4-15).

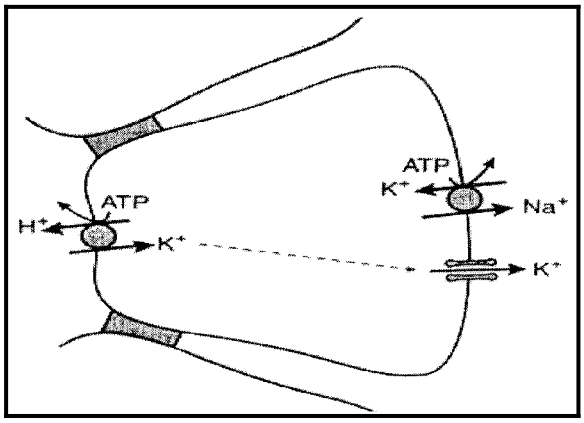


Fig. (4-15): Mechanism of K^+ reabsorption by intercalated cells.

- **K^+ Secretion**: Occurs in principal cells.

Principal cells in the late distal tubule and cortical collecting tubule secrete K^+ into the tubular lumen.

- Is variable and depends on dietary K^+, aldosterone level, acid-base status and urine flow rate.

- **Mechanism of K^+ secretion: (Fig. 4-16).**
- *At the basolateral membrane:*

Na^+ - k^+ moves Na^+ into the interstitium, while K^+ moves into the interior of the cell.

This pump mai ation.

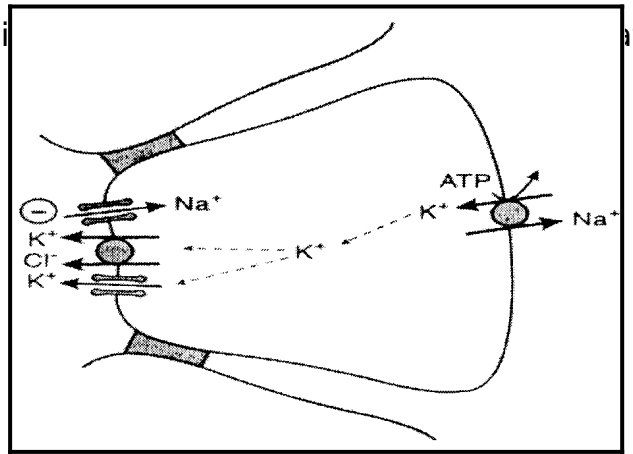


Fig. (4-16)

- *At the luminal membrane:*

  K^+ diffuses through the luminal membrane from the interior of the cell into the tubular fluid in view of electrochemical gradient.

  K^+ diffuses through K^+ - channels and via K^+ - Cl^- co-transporter.

  Tubular secretion of K^+ is under effect of aldosterone, acting on P cells of late distal tubule and collecting duct.

- ***Regulation of Tubular Potassium Secretion:*** (Distal tubule and collecting duct).

  1. Plasma Potassium Concentration

  The rate of K^+ secretion increases as plasma K^+ concentration increases.

  *** Mechanism:**

  a) *Increased activity of Na^+ - K^+ ATPase by:*

  i. Direct effect of extracellular K^+ level.

  ii. ii) Increased aldosterone secretion (by rise of K^+ level).

  b) *Increased number of K+ channels in the luminal membrane by* aldosterone.

  2. Flow rate in the distal tubule:

  A rise in distal tubular flow rate stimulates K^+ secretion: With increased tubular flow rate, the secreted K^+ is flushed down the tubule, so K^+ does not rise in the tubule➔ enhance the diffusion gradient of K^+ from the cells. This is one of several

reasons why diuretic therapy can lead to K^+ depletion.

3. **Aldosterone:** increase K^+ secretion. Hyperaldosteronism increases K^+ secretion and causes hypokalemia.

   Hypoaldosteronism decreases K^+ secretion and causes hyperkalemia.

4. **Acid - Base Status:**

   a) Acidosis: Reduce K^+ secretion.

   * **Mechanism:**

   • Inhibition of Na^+ - K^+ ATPase➔ decrease intracellular K^+ concentration.

   • In acidosis, there is efflux of K^+ and uptake of H^+ from ECF ➔decrease intracellular K^+ concentration in the cortical and collecting duct cells (P-cells).

   • The decreased intracellular K^+ concentration leads to decreased cell to lumen K^+ concentration gradient ➔ decrease K^+ secretion.

   b) *Alkalosis increases K^+ secretion.*

Secretion of Hydrogen & Reabsorption of Bicarbonate

Site: H^+ is secreted in all parts of the renal tubule except the descending and ascending thin limbs of the loop of Henle.

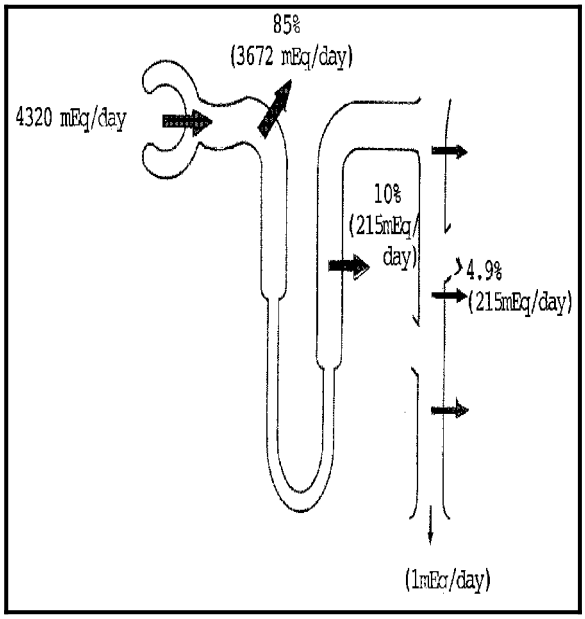


Fig. (4-18): HCO_3^- reabsorption by renal tubule.

For each H^+ secreted, one bicarbonate is reabsorbed. Bicarbonate is reabsorbed mainly by the proximal tubule (85%), thick ascending loop of Henle (10%) and collecting duct (4.8%) (Fig. 4-18).

The renal tubules are poorly permeable to HCO_3^-. However HCO_3^- which is reabsorbed is formed by the tubular epithelium from CO_2 as follows:

- CO_2 either diffuses into the tubular cell from the blood or is formed by metabolism in tubular epithelial cell.
- CO_2 combines with H_2O under the influence of carbonic anhydrase to form H_2CO_3.
- H_2CO_3 dissociates into H^+ and HCO_3^-.
- H^+ are secreted from the tubular cell into the tubular fluid, where it is buffered by :
  1) Bicarbonate buffer in the tubular fluid.
  2) Phosphate buffer in the tubular fluid.
  3) Ammonia synthesized by tubular epithelium.
- HCO_3^- generated in the cell moves into the renal interstitium by diffusion.

Mechanism of H^+ secretion:

1. Secondary active transport:

Occurs in the proximal tubule, loop of Henle and initial part of distal tubule.

The secondary active transport of H^+ occurs by counter-transport mechanism utilizing an antiport carrier at the luminal borders of the tubular cells. This carrier binds H^+ and Na^+. Na^+ diffuses into the tubular cell while H^+ into the tubular lumen. (Fig. 4-19).

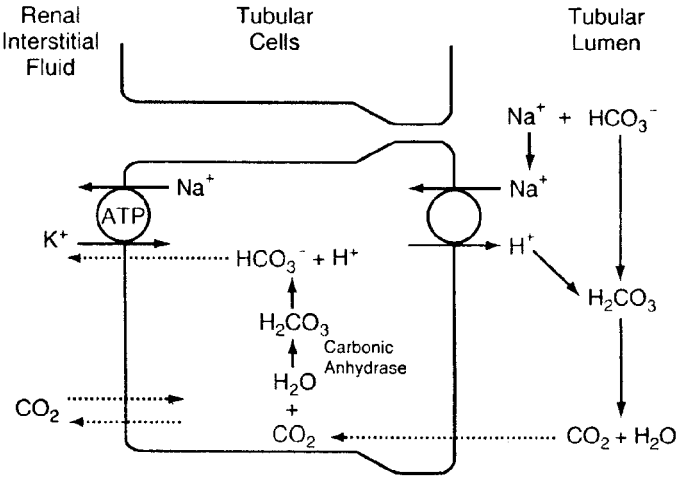


Fig. (4-19)

2. Primary active secretion:

- Occurs in the late distal tubule and collecting ducts.
- It is Na^+ - independent.
- It is stimulated by aldosterone, which can be increased up to 900 folds.
- H^+ is transported actively by H^+-ATPase pump at the luminal membrane of the intercalated cells. (Fig. 4-21).

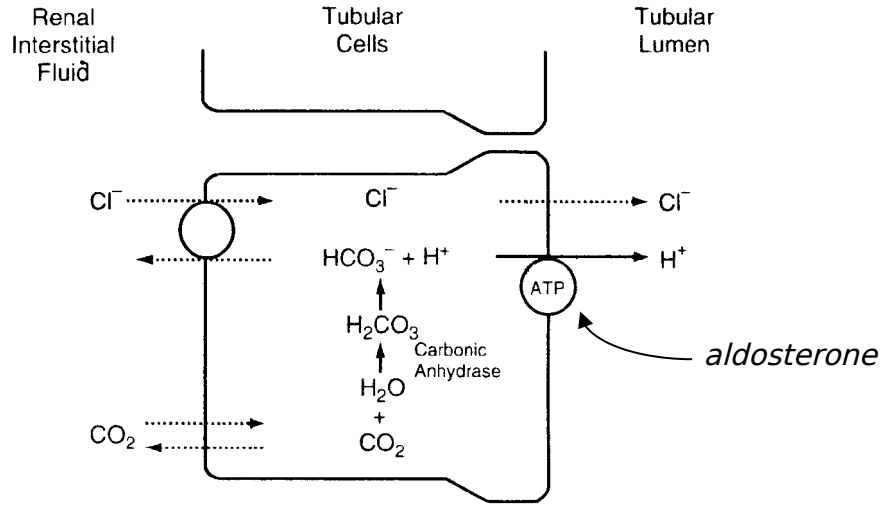


Fig.(4-20)

Fate of H^+ secreted:

The secreted H^+ is buffered by the buffers in the tubular fluid.

1-<u>In the PCT:</u>

Buffering by the $NaHCO_3$ in the tubular fluid.

$H^+ + HCO_3^- \rightarrow H_2CO_3$ (in the lumen)

Na^+ is reabsorbed in exchange with H^+.

H_2CO_3 dissociate into H_2O and CO_2 by carbonic anhydrase at the luminal borders of the tubular cells of the proximal tubule only.

pH of tubular fluid in PCT is changed very little since most H^+ is removed from the tubule by binding with HCO^-_3.

2. <u>In the Distal tubule and collecting duct</u>:

a) **<u>Buffering by phosphate buffer</u>**: . 30 - 40 mEq of Na_2HP0_4.are available per day.

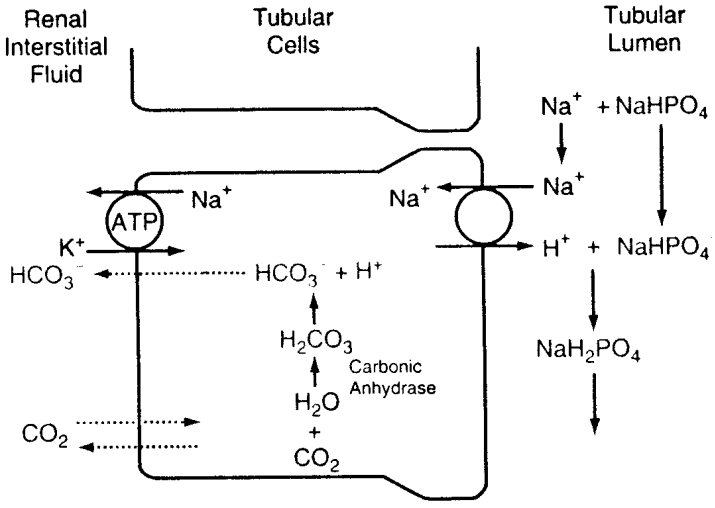
It is concentrated by time it reaches distal tubule and collecting duct.

H^+ is buffered as follows:

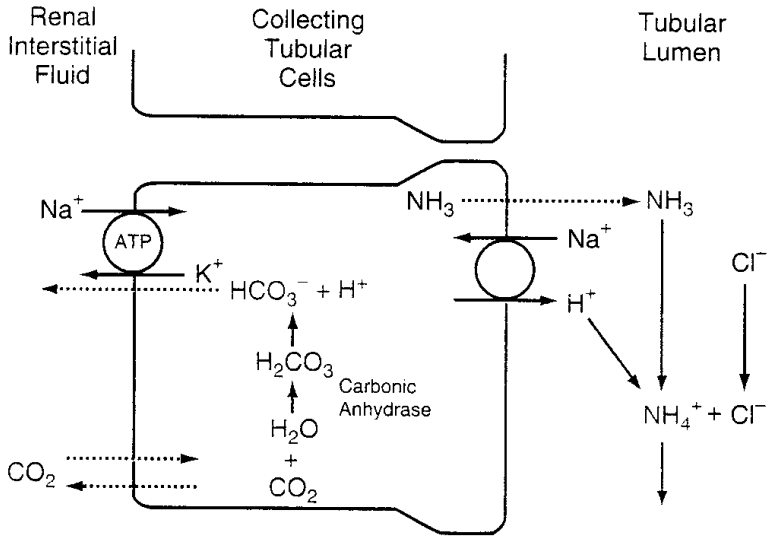
$H^+ + Na_2HPO_4 \rightarrow NaH_2PO_4 + Na^+$

NaH_2PO_4 is excreted accounting for most of the titratable acidity in urine Na^+ is reabsorbed together with intracellular HCO_3^-. (Fig. 4-21)

This process results in secretion of H+ and net reabsorption of newly svnthesized HCO_3^-



b) Buffering by ammonia (NH_3). (Fig. 4-22):



NH_3 is formed in most parts of the renal tubule specially the distal tubule and collecting duct from glutamine.

$$Glutamine \xrightarrow{Glutaminase} Glutamic\ acid + NH_3$$

NH_3 is lipid-soluble and diffuses into the tubular fluid. H^+ combines with NH_3 to form NH_4^+, which is then excreted in urine together with Cl^- (from NaCl) forming NH_4Cl. Na^+ are reabsorbed into the renal interstitium together with the HCO3 from the tubular cells.

Importance of H^+ buffering:

H^+ secretion in the distal tubule and collecting ducts occurs as

long as the pH of the fluid in these segments is above 4.5 which is the limiting pH for H^+ secretion. If the secreted H^+ is not buffered, this pH would be reached rapidly leading to stoppage of further H^+ secretion.

Factors affecting acid secretion:

1) Aldosterone: increase H^+ and K^+ secretion.

2) Intracellular PCO_2: when PCO_2 is high (respiratory acidosis) more intracellular $H_2CO_3$is available and H^+ secretion is enhanced.

3) K^+ concentration in the cells:

a) K^+ depletion in the cells enhances H^+ secretion.

b) K^+ excess in the cells inhibits acid secretion.

Summary of Hormones that Act on the Kidney

Hormone	Stimulus for Secretion	Time Course	Mechanism of Action	Actions on Kidneys
PTH	↓plasma $[Ca^{2+}]$	Fast	Basolateral receptor Adenylate cyclase→ cAMP urine	↓ Phosphate reabsorption (proximal tubule) ↑Ca^{2+} reabsorption (distal tubule) Stimulates 1α hydroxylase (proximal tubule)
ADH	↑ Plasma osmolarity ↓ Blood volume	Fast	Basolateral V_2 receptor Adenylate cyclase cAMP	↑ H_2O permeability (late distal tubule and collecting duct principal cells).
Aldosterone	↓blood volume (via rennin-angiotensin II) ↑plasma $[K^+]$	Slow	New protein synthesis	↑Na^+ reabsorption (distal tubule principal cells). ↑K^+ secretion (distal tubule principal cells).
ANP	↑atrial prsessure	Fast	Guanylate cyclase cGMP.	↑ GFR ↓Na^+ reabsorption
Angiotensin II	↓blood volume (via renin)	Fast		↑Na^+-H^+ exchange & HCO_3^- reabsorption (proximal tubule).

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